Theoretical Optimization of Analyte Collection in Analytical Supercritical Fluid Extraction

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Key Words

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Summary

Optimizing the extracted analyte collection step in analytical supercritical fluid extraction (SFE) is of key importance in achieving high analyte recoveries and extraction efficiencies. Whereas the extraction step in SFE has been well characterized both theoretically and experimentally; the analyte collection step after SFE has few theoretical guidelines, aside from a few empirical studies which have appeared in the literature. In this study, we have applied several theoretical approaches using experimental data to optimize analyte trapping efficiency in SFE. A vapour-liquid equilibrium model has been formulated to predict the trapping efficiency for extracted solute collection in a open collection vessel. Secondly, a simple solution thermodynamic model for predicting solute (analyte) activity coefficients in various trapping solvents has been shown to have utility in predicting collection efficiencies. Finally, effective trapping efficiency after SFE using sorbent media is related to the extent of analyte breakthrough on the sorbent-filled trap after depressurization of supercritical fluid. Using experimental data determined via physico-chemical gas chromatographic measurements (i. e., specific retention volumes), we have shown the relationship between analyte breakthrough volume off of the trapping sorbent and volume of depressurized fluid through the collection trap. The above theoretical guidlines should prove of value to analysts in designing and optimizing the best conditions for trapping analytes after extraction via analytical SFE.

Introduction

Analytical supercritical fluid extraction (SFE) is becoming a routine technique in many analytical laboratories for the extraction and cleanup of environmental, food and pharmaceutical samples. Optimization of the extraction step in analytical SFE has been relatively well characterized both theoretically [1] and experimentally [2]. Theoretical explanations of solute (analyte) solubility in supercritical fluids have been predicted by phase [3] and thermodynamic [4, 5] considerations, and kinetic models [6, 7] have also been applied to optimize the rate and efficiency of the SFE.

However the study or optimization of the collection stage in analytical SFE and been relatively ignored by researchers. Some empirical and experimental-based studies have been reported by various researchers, particularly Taylor and colleagues [8], who have studied the impact of various experimental parameters on analyte trapping efficiency. Miller, et al. [9] have reported on the solventless collection of analytes by rapid epressurization after static SFE, while King and coworkers [10] have routinely used the principle for oil/fat collection after SFE.

There are several modes for trapping extracted analytes in analytical SFE and each is effected by temperature. The most utilized options are open vessel, liquid and sorbent trapping of analytes. Taylor and coworkers have studied collection efficiency using both neat and modified collection solvents [11-13], for both model test solutes and fat soluble vitamins. Similarly, Langenfeld, et al. [14] measured the effect of collection solvent parameters as well as extraction cell geometry for over 65 different compounds in 5 different solvents. More recently, Vejrosta, et al. [15] have reported optimizing the collection device, for low boiling compounds having a vapour pressure similar to the collection solvent, where significant analyte losses can occur.

The use of solid adsorbent-based traps after analytical SFE has also been very popular. Again Taylor and coworkers [16-18] have conducted studies to measure the trapping efficiencies of various adsorbents with neat and modified supercritical carbon dioxide (SC-CO_2), the variance in the trapping capacity for different types of solid phases, and the effect of trap temperature on
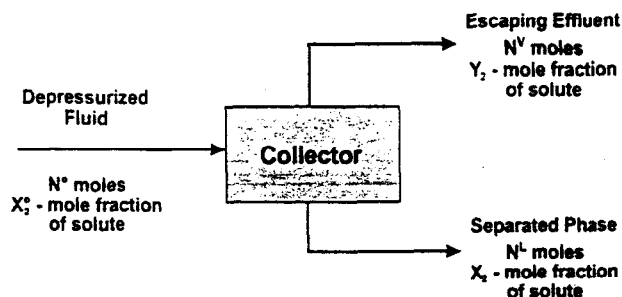
Figure 1
Model for solute (analyte) loss in effluent via open vessel collection during SFE.

Table 1. Ratio of Vapor Pressures of the Collection Solvent to that of Solute (Analyte) (P^s_1/p^s_2) at 25 °C.

Solvents	Solutes		
	Naphthalene	Phenol	Methyl Methacrylate
Benzene	$2.4 \cdot 10^2$	$2.7 \cdot 10^2$	2.4
Methylene Chloride	$1.1 \cdot 10^3$	$1.2 \cdot 10^3$	10.8
Diethyl Ether	$1.4 \cdot 10^3$	$1.5 \cdot 10^3$	13.7
Methanol	$3.2 \cdot 10^2$	$3.6 \cdot 10^2$	3.2
Hexane	$3.8 \cdot 10^2$	$4.2 \cdot 10^2$	3.8
Carbon Dioxide	$1.3 \cdot 10^5$	$1.4 \cdot 10^3$	$1.3 \cdot 10^3$

analyte recovery. Chaudot et al. [19] also studied the effect of modifier content on the trapping efficiencies of various adsorbents, and showed that analyte retention was possible even when the modifier content of carbon dioxide was quite high (e. g., 10 % methanol).

The trapping of volatile analytes using solid phase traps is always more problematic, and toward that end, King and Taylor [20] have determined breakthrough volumes from physicochemical chromatographic measurements using low pressure carbon dioxide as an eluent. There is also a considerable literature from the environmental analysis community [21, 22] with regards to the use of sorbents to isolate volatile and semivolatile compounds from the atmosphere, to aid the analyst in establishing optimum conditions for sorbent trapping relevent to SFE. Such sorbate breakthrough volume studies [23, 24] are pertinent to minimizing analyte losses during trapping of analytes in SFE; although there is paucity of such data for a carbon dioxide atmosphere.

In this study we have utilized available experimental data and several simple models to predict and optimize the trapping efficiency of analytes during SFE. These include invoking a simple vapour-liquid equilibrium model to predict capture efficiency in open vessel trapping, the use of predicted (or actual) activity coefficient data to optimize collection efficiency in liquid trapping mode, and utilizing analyte breakthrough volume data

determined by physicochemical gas chromatography for selecting optimal trapping conditions for collection on sorbents.

Experimental and Theoretical Calculations

Modeling of Solute Collection in an Empty Collection Vessel

The trapping of a solute dissolved in a supercritical fluid undergoing depressurization into any empty trap or collection vessel can be be viewed as a single stage vapor-liquid separation process. As shown in Figure 1, the depressurized fluid containing N^o moles or X^o_2 mole fraction of solute is separated in the open collection vessel into the escaping effluent containing N^V moles of solute or Y_2 mole fraction of solute. The separated or collected phase contains N^L moles of solute corresponding to X_2 mole fraction of solute.

The phase equilibrium relationship in the vapor phase therefore can be written as:

$$Y_2/1 - Y_2 = p^s_2 \, \gamma_2 X_2 / p^s_1 \, \gamma_1 \, (1 - X_2) \tag{1}$$

and solving for Y_2, and invoking Raoult's Law:

$$Y_2 = 1/1 + p^s_1 \, (1 - X_2)/p^s_2 X_2 \tag{2}$$

we have for dilute solutions:

$$Y_2 = (p^s_2/p^s_1)X_2 \tag{3}$$

Therefore, the solute (analyte) loss to the vapour state in percent is:

$$10^2 \, (Y_2 N^V/X^o_2 N^o) = 10^2 \, [1 - N_L/N^o/1 + (p^s_1/p^s_2 - 1)N^L/N^o] \tag{4}$$

where p^s_i = vapour pressure of the pure ith liquid

γ_i = activity coefficients of the ith solute

The solute loss (that not collected) is a function of the extent of concentrating (N^L/N^o) and the ratio of collection solvent to solute vapor pressures (p^s_1/p^s_2). To illustrate the importance of the solute to solvent vapor pressures, three solute vapor pressures were calculated and compared as a ratio with five common liquids, plus carbon dioxide at 25 °C as shown in Table 1. Thus, for a 25-fold increase in concentration $(N^L/N^o = 1/25)$, and a vapor pressure ratio of 3, for methyl methacrylate in benzene, methanol, and hexane respectively, 89 % of the solute would be lost. For a vapor pressure ratio of 14 (e. g., methyl methacrylate in diethyl ether or methylene chloride), 63 % of the solute would be lost. However, for the case of methylene chloride separating from carbon dioxide (vapor pressure ratio of 1.3×10^3), only 1.7 % of the solute would be lost. This illustrates the nice phase separation of the solute afforded by using carbon dioxide as the extraction solvent upon depressurization of the resultant mixture.

Activity Coefficient Calculations/Correlations

The activity coefficient of a solute (analyte) in solution (liquid) is a measure the escaping tendency of that solute

from the liquid media. As such, this basic physico-chemical solution thermodynamic parameter can be related to the capture efficiency of a particular solvent for a solute (analyte) during extract collection while conducting SFE. One of simplest methods for calculating activity coefficients of solutes in solution is via regular solution theory with perhaps an entropic correction factor for the size disparity between the solvent and solute moleclues. This can be facilitated using Eq. (5) below where the logarithm of the total activity coefficient, γ_T is equal to the combined sum of the enthalpic and entropic contributions to γ, γ_E and γ_S, by:

$$\ln \gamma_T = \ln \gamma_E + \ln \gamma_S = V_1 (\delta_1 - \delta_2)^2 / RT \qquad (5)$$

where V_1 = solute molar volume

δ_1 = solute solubility parameter

δ_2 = solvent solubility parameter

R = gas constant

T = absolute temperature in °K

Solubility parameters for the various solutes were calculated for consistency using the functional group contribution method of Fedors [25]. Typical solute solubility parameters are tabulated in Table II along with the solubility parameters for the relevant collection solvents. The solutes and solvents were chosen to give an range of corresponding solute and solvent solubility parameters embracing both non-polar and polar solutes/solvents. These were then used to calculate various solubility parameter differences, $(\delta_1 - \delta_2)$, enthalpic activity coefficients, and total activity coefficients. These computed parameters were then plotted versus collection efficiencies from SFE experiments as reported by Langenfeld, et al. [14] for the corresponding solutes and solvents listed in Table II to see if this had any predictive value for choosing the best collection solvent.

In addition, the effect of a γ_S term, $\ln \gamma_S = \ln r + (1-1/r)$, where r = ratio of the molar volume of V_1/V_2, and V_2 is the molar volume of the fluid, according to Flory-Huggins theory [26] was also computed. It should be noted that negative values of $\ln \gamma$ are possible for cases where the solute (analyte) is readily dissolved in the chosen liquid solvent. The computed γ's were than averaged as a function of analyte recovery (%) to ascertain whether a distinct relationship exists between the recovery of the analyte in a particular solvent and the solute activity coefficients.

Analyte Breakthrough Volumes – Calculations and Correlations

The 50 % breakthrough volume for an analyte (sorbate) on an adsorbent is conventionally used as a measure of retention of the sorbate on an adsorption column. In the region approximating the zero surface coverage of the sorbate on the sorbent, the breakthrough volume is

Table II. Solubility parameters of solutes (analytes) and collection solvents.

Solutes	δ*	Solvents	δ*
Phenol	12.27	n-Hexane	7.28
2-Chloroethyl Ether	9.48	Methanol	14.47
1,2-Dichlorobenzene	10.02	Methylene Chloride	9.92
4-Methylphenol	10.22	Chloroform	9.29
Nitrobenzene	10.02	Acetone	9.78
Isophorone	9.39		
Dimethyl Phthalate	10.7		
3-Nitroaniline	12.22		
Diethyl Phthalate	10.07		
Phenanthrene	9.78		
Dibutyl Phthalate	9.29		
Dioctyl Phthalate	7.92		

* $(cal/ml)^{1/2}$

equivalent to the peak maximum specific retention volume of an injected analyte on a chromatographic (sorbent) column. The calculation of the specific retention volume, V^T_g, is given by Eq. (6) below as:

$$V^T_g = j F_c (t_r - t_a)/W_A \qquad (6)$$

where F_c = flow rate of the carrier fluid at column temperature

j = James-Martin compressibility factor

t_r = peak maximun retention time

t_a = retention time for non-sorbed solute

W_A = weight of adsorbent

The specific retention volume of the analyte can be measured very precisely on a modified gas chromatograph using small tubes filled with an appropriate sorbent as columns (traps). For details on the experimental measurement of V^T_g see [20, 26]. Specific retention volumes in this way were measured for at least four different temperatures for different classes of analytes adsorbing on Tenax-TA an XAD-2 resin using carbon dioxide as the carrier fluid, thereby permitting the relationship to be established between V^T_s and the reciprocal of the absolute temperature (Van't Hoff plots). Correlation coefficients for such plots were typically above 0.995, indicating a high degree of linearity over the experimental temperature range utilized. Extrapolation on these highly linear plots of the V^T_s versus 1/T_c to room temperature (20–25 °C) gave the V^T_g's expected at ambient conditions.

As shown in Figure 2, for n-propylbenzene adsorbing on Tenax-TA, the curves are highly linear, ($r^2 = 0.99987$) permitting extrapolation of the breakthrough volumes (V^T_g) to values corresponding to those used for trapping conditions in SFE. It should be appreciated that the linear dependence of the (V^T_g) for n-propylbenzene on Tenax-TA resin is not the same for the elution of an analyte from the sorbent using carbon dioxide versus a typical gas chromatographic carrier fluid, such as he-
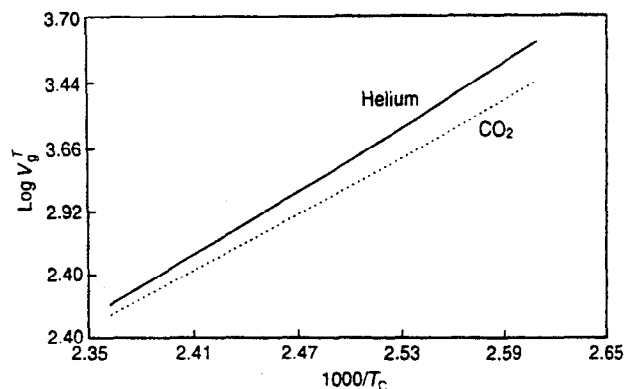
Figure 2

Log V^T_g versus $1/T_c$ for n-propylbenzene adsorbing on Tenax-TA from carbon dioxide and helium.
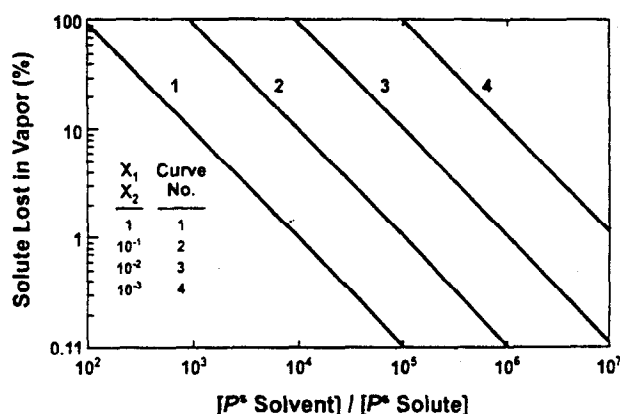

Figure 3

Solute loss in collector effluent as a fraction of the relative volatility for various degrees of solvent removal.

lium. Figure 2 indicates that breakthrough volumes from a sorbent are reduced in the presence in carbon dioxide relative to those found for helium as a carrier gas, even for volatile compounds on the above sorbent. This trend is consistent with the larger negative mixed virial coefficients (B_{12}) exhibited by solutes in carbon dioxide relative to those found for other solute-gas systems [27], as well as greater solvating or displacing influence of CO_2 on the sorbent surface [28].

Results and Discussion

Predicting the Loss of Solute in a Open Collection Vessel (Neat Collection of the Analyte)

Figure 3 is a generalized plot of percent solute loss into the vapor phase versus the ratio of the saturated vapor pressure of the solvent to that of the solute as predicted by Eq. (4). Using this relationship, four specific ratios of solute to solvent mole fractions, ranging from unity to 10^{-3} were calculated and are shown in Figure 3. Clearly,

higher losses of analyte occur as the saturated vapor pressure ratio of solvent to solute increases. Therefore, Figure 3 can be used to assess, based on relative solute/solvent vapor pressures, the anticipated solute loss contributing to reduced analyte collection efficiency, and what solutes (analytes) can be collected successfully.

Therefore, for this single equilibrium stage model, to obtain an extract containing less than 10 mole percent solvent (e. g., carbon dioxide) and a corresponding loss of only 1 % of solute, a vapor pressure ratio of 10^5 is required. Recalling the results from Table I, it can be seen that most typical liquid collection solvents cannot meet such a criteria, but precipitation of the higher vapor pressure solutes, such as phenol or naphthalene from carbon dioxide would give a negligible loss of solute into the vapor phase. For the case of methyl methacrylate and carbon dioxide, the vapor pressure ratio is too low to meet the above criterion, however this situation can be improved substantially by cooling the trap to say -25 °C where the equilibrium mole fraction in the vapor state would be reduced considerably.

Predicting Collection Efficiency in Liquid Solvents

Parameters such as the difference between the solubility parameters of the solute and solvent or the activity coefficient of the solute in the collection solvent, have the potential for correlation with the solute collection efficiency after SFE, since they are a measure of solute-solvent interaction, which should influence solute collection efficiency. Initial attempts to correlate the collection recoveries reported by Langenfeld, et al. [14] with the square of the difference in solubility parameters of the solute and collection solvent showed considerable scatter, but a downward trend when percent analyte recovery versus the square of the difference between the solubility parameters was apparent.

Likewise, use of just the logarithm of the enthalpic activity coefficient, which is proportional to the solubility parameter difference between the solute and solvent. also showed that low analyte recovery was consistent with an increasing value of γ. A general decreasing trend of solute recovery with the logarithm of the total activity coefficient was observed, although there was still some scatter in the resultant plot. This trend is however consistent with decreasing molecular interaction (or attraction) between the solute and solvent molecules.

Using a multipoint averaging method on the data in Table II provided a much more consistent trend than those observed above. In this case, the values of the first six activity coefficients were averaged as well as their corresponding recoveries. Then, the following six activity coefficients and recoveries were averaged, the process was repeated until all activity coefficients and recoveries are averaged; each graphical data point representing six values. The averaged recovery was then plotted against the averaged activity coefficients. This is

shown in Figures 4 and 5 where one can see that as the solubility parameter difference increases (or the logarithm of the total activity coefficient increases) there is a corresponding decrease in the solute recovery that can be correlated. The addition of the Flory-Huggins entropic term shows solute activity coefficients ranging from –0.6 to over 1.5, reflecting a analyte capture efficiency ranging from 92 % to approximately 65 %. Clearly, the larger the activity coefficient of the solute in the collection solvent, the worse the collection efficiency becomes.

Therefore, by knowing the solubility parameters of the solute and solvent respectively, one can approximate the escaping tendency of the analyte from the collection solvent, and thus chose collection solvents that should be optimal for isolating a target analyte(s). It is also possible to utilize reported activity coefficient in the literature for specific solutes (analytes) interacting with a solvent for this purpose. The Dechema activity coefficient compendium [29], tabulating activity coefficients at infinite dilution (a condition which occurs during SFE collection due to the small solubilities of most solutes in supercritical fluids), provides one source of this data. In addition, γ's measured by thermodynamic gas chromatographic studies [30] at infinite dilution in volatile stationary phases can also be used to assess the capture efficiency of a chosen collection solvent.

Predicting Optimal Conditions for Sorbent Phase Trapping in SFE

It has been previously shown that chromatographically-measured breakthrough volumes, V^T_g, can be linearly correlated with the boiling point of the analyte within a distinct chemical class of solutes [23]. This is shown in Figure 6 where extrapolated values of V^T_g on Tenax-TA have been plotted versus the boiling point of various chlorinated hydrocarbon solutes used in the chromatography adsorption experiments. Similar correlations exist for n-alkanes, alcohols, aromatic compounds, and aliphatic aldehydes., although small differences exist for each class of solutes (embracing Class A, B, and D sorbate types as classified by Kiselev [31]) with respect to their slopes and intercepts on such plots. The existence of these type of correlations permits the chromatographic breakthrough volumes for any solute to be estimated from knowledge of its boiling point, and its trapping efficiency to be maximized with respect to avoiding analyte loss (breakthrough) from a solid sorbent trap.

When the above linear correlations of V^T_g for different solute classes are plotted versus the respective boiling points for the various analytes, a general linear correlation results as shown in Figure 7. This type of correlation again can be used to estimate the breakthrough volume for a analyte from it boiling point, and can be combined with the previously-mentioned Van't Hoff plots to estimate the V^T_g breakthrough values at any trapping temperature. For example, if we run our SFE experiment at

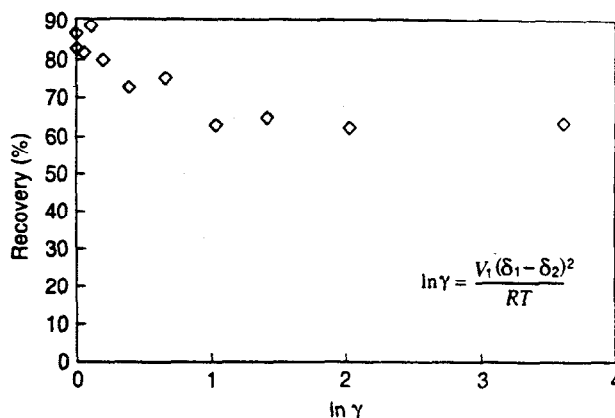**Figure 4**

Solute collection efficiencies versus activity coefficients (excluding entropy term) of organic solutes (analytes) in collection liquids.
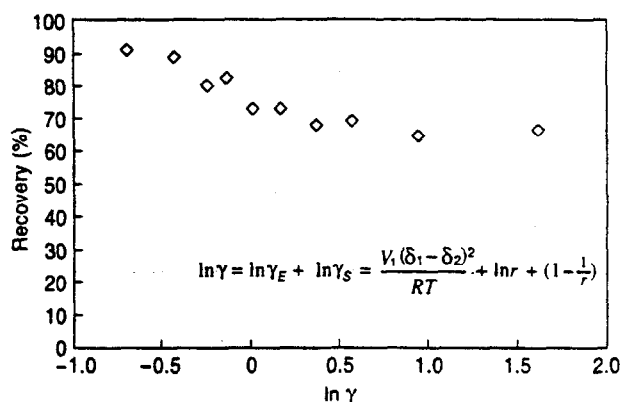

Figure 5

Solute collection efficiencies versus activity coefficients of organic solutes (analytes). In collection liquids.
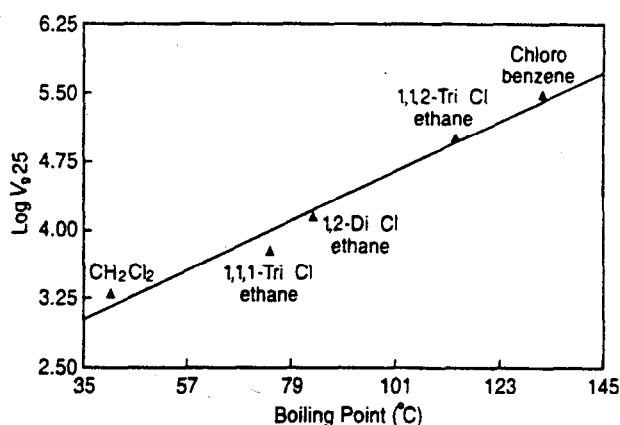

Figure 6

Log V^T_g (25 °C) versus boiling points of chlorinated hydrocarbons on Tenax-TA with carbon dioxide.
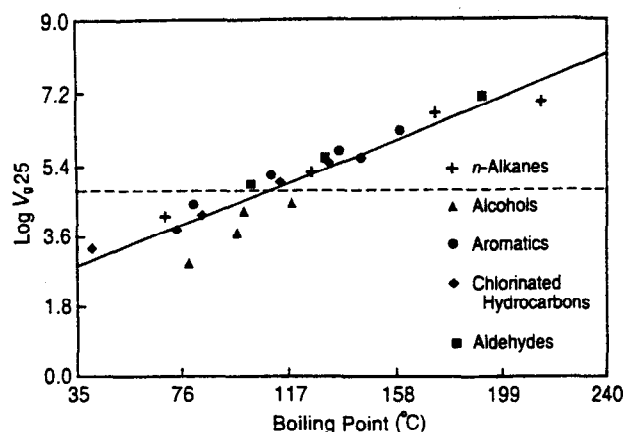
Figure 7

Log V^T_g (25 °C) versus boiling points of assorted analytes (sorbates) classes on Tenax-TA with carbon dioxide.

An expaned CO_2 flow rate of 2 $L \cdot min^{-1}$ using 2 grams of Tenax-TA for trapping, for a 30 minute extraction time, than the total volume of CO_2 used and expanded is 60 $L \cdot g^{-1}$ of adsorbent at 25 °C and 1 atm. This corresponds to the dashed line in Figure 7. Those analytes exhibiting a higher breakthrough volume then this value (e. g., 172 $L \cdot g^{-1}$ for n-octane), will thus be retained on the trapping adsorbent; while those analytes exhibiting a lower V^T_g than 60 $L \cdot g^{-1}$, will breakthrough the trap and not be captured efficiently. For example, all of the alcoholic solutes in Figure 7 would not be retained in the trap under the above specified conditions, however based on the above correlations, lowering the trap temperature to –25 °C, will retain all of the alcohols but ethanol on the Tenax-TA-filled trap. Such correlations are extremely useful in understanding the principles involved in solid phase trapping for SFE, and should be used as a first step in optimizing the trapping of target analytes.

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